REMARKS/ARGUMENTS

Status of the Claims

Claims 71 and 76-80 were rejected. Claims 1-70 were previously canceled without prejudice or disclaimer. To further prosecution, claim 71 has been amended to incorporate the subject matter of claim 78 and now specifically recites that "at least about 50% of the discrete dried vaccine particles have a volume diameter within about 80% of the mean." Further support for this claim amendment can be found in the specification as originally filed at, for example, paragraphs [0034], [0036], and [0042]. Accordingly, no new matter has been added by way of this claim amendment, and claim 78 has been canceled. Applicants expressly reserve the right to file a continuation or divisional application or to take other such appropriate action to seek protection of the canceled subject matter.

Claims 71, 76, 77, 79, and 80 are now pending in the present application. Reexamination and reconsideration of the claims are respectfully requested in view of the claim amendments and the following remarks. The Examiner's rejections in the Office Action are addressed below in the order set forth therein.

The Rejection of the Claims Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 71 and 76-80 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2002/0120228 (hereinafter "the '228 patent application publication") in view of U.S. Patent Application Publication No. 2006/0024322 (hereinafter "the '322 patent application publication"). As noted above, the subject matter of claim 78 has been incorporated into claim 71 to expedite prosecution, and, therefore, claim 78 has been canceled. This rejection is respectfully traversed with respect to the pending claims.

Independent claim 71 as previously presented was drawn to a particulate recombinant Staphylococcal enterotoxin B (rSEB) vaccine composition made by a method comprising atomizing a liquid rSEB formulation to produce an atomized formulation, freezing the atomized rSEB formulation to form solid particles, and drying the solid particles to produce discrete dried particles of the rSEB vaccine composition. Dependent claims 76-80 further recited specific particle size ranges and particle size distributions for the discrete dried particles of the claimed

particulate rSEB vaccine compositions. The Examiner maintains that these claims are obvious in view of the '228 patent application publication and the '322 patent application publication.

The '228 patent application publication discloses a gel-forming, free-flowing powder suitable for use as a vaccine, prepared by a spray-drying or spray-freeze-drying process. The Examiner maintains that the particle size ranges recited in claims 76-80 are taught by the cited reference. As acknowledged by the Examiner, however, the '228 patent application publication does not teach or suggest an rSEB vaccine composition comprising discrete dried particles of any size.

The '322 patent application publication, which was cited in the previous Office Action mailed January 25, 2007, discloses a Staphylococcal enterotoxin B (SEB) vaccine, particularly a solid vaccine formulation produced by *lyophilization*. See paragraph [0048] of the cited reference. The Examiner concludes that the teachings of the '228 patent application publication and the '332 patent application publication can be combined to arrive at the claimed particulate rSEB vaccine compositions. Applicants respectfully disagree with the Examiner's conclusions.

Although Applicants do not concede that the claims as previously presented are rendered obvious by the cited references, to expedite prosecution claim 71 has been amended to recite that at least about 50% of the discrete dried particles have a volume diameter within 80% of the mean, as previously included in now canceled claim 78. The Examiner maintains that this particle size range would necessarily be achieved by the method disclosed in the '228 patent application publication (see page 5 of the Final Office Action mailed September 11, 2007). The cited reference discloses a broad range of particle sizes (i.e., 0.1 to 250 μm), but, contrary to the Examiner's assertions, at no point does the '228 patent application publication teach or even suggest that at least 50% of the resultant population of discrete dried particles have a volume diameter within 80% of the mean, as recited in all of the pending claims. In fact, the Applicants of the '228 patent application publication explicitly state that "[t]he average particle size of the powders according to the present invention can vary widely." See paragraph, for example, page 4, paragraph [0058].

The disclosure of the '322 patent application publication does not cure the deficiencies of the '228 patent application publication. As noted in the previous Response filed June 25, 2007,

the '322 patent application publication is drawn to a solid vaccine formulation produced by lyophilization. In contrast to the discrete dried vaccine particles described in the specification and recited in the present claims, the desired end product of lyophilization is a "cake" and not a collection of discrete particles. See, for example, "*Lyophilization: Introduction and Basic Principles*" (Thomas A. Jennings, ed.; Interpharm Press 1999), portions of which were previously submitted for the Examiner's consideration. Accordingly, as the methods taught by the '322 patent application publication produce a dried vaccine "cake," the cited reference necessarily does not disclose an rSEB vaccine composition comprising discrete dried vaccine particles, wherein the discrete particles have a volume diameter within about 80% of the mean, as recited in all of the pending claims.

Establishing a *prima facie* case of obviousness requires assessment of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), which provides the framework for applying the statutory language of § 103. Under the "Graham Factors," the Examiner is required to:

1. Determine the scope and content of the prior art;
2. Ascertain the differences between the prior art and the claims at issue;
3. Resolve the level of ordinary skill in the pertinent art; and
4. Consider any relevant secondary considerations.

Moreover, a *prima facie* case of obviousness under 35 U.S.C. § 103(a) requires that the combination of references places the claimed subject matter in the public domain prior to Applicants' date of invention. See *In re Zenitz*, 333 F.2d 924, 142 USPQ 158 (C.C.P.A. 1964). Thus, establishing a *prima facie* case of obvious requires that the cited references can be combined such that each and every element of the claimed invention is taught, explicitly or implicitly, by the references and that a reasonable expectation of success exists in such a combination. In the instant case, neither of the cited references discloses, explicitly or implicitly, a particulate rSEB vaccine composition made by a method comprising the steps of atomizing a liquid rSEB formulation to produce an atomized formulation, freezing the atomized formulation to form solid particles, and drying the solid particles to produce discrete dried particles of the rSEB vaccine composition, *wherein the discrete dried particles have a volume mean diameter within about 80% of the mean*. For the reasons set forth above, the disclosures of the '228 patent

application publication and the '322 patent application publication simply cannot be combined to arrive at the claimed particulate rSEB vaccine composition. The '228 patent application publication does not cure the deficiencies of the '322 patent application, and, as such, the pending claims are not obvious in view of the cited references.

Although Applicants maintain that a *prima facie* case of obviousness has not been established in the present case, evidence of secondary considerations such as unexpected results or unforeseen advantageous properties of the claimed particulate rSEB vaccine composition can rebut a *prima facie* case of obviousness. See *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987); *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). In particular, independent claim 71 and all claims dependent thereon have been amended to recite a particulate rSEB vaccine composition having a well-defined particle size distribution (i.e., "wherein at least about 50% of the discrete dried particles have a volume diameter within about 80% of the mean"). Vaccine compositions comprising a population of dried solid particles that display a well-controlled, uniform particle size distribution are advantageous for a number of reasons. Uniform particle size improves bioavailability and pharmacokinetics of the vaccine composition and reduces the potential for particle agglomeration, thereby facilitating accurate dosing to patients when the vaccine composition is administered intranasally as a powder or intradermally following reconstitution of the particulate vaccine composition in a pharmaceutically acceptable carrier. In the exemplary case of intranasal delivery of a vaccine composition of the invention, the well-controlled particle size range recited in the claims permits the adherence of the particles to the nasal lining or sinuses, where the vaccine particles are rapidly absorbed into the bloodstream, and minimizes delivery of the composition into the pulmonary system where it may cause negative, unwanted side effects. The accurate intranasal targeting of the claimed rSEB vaccine also reduces the time required to mount an effective antibody response. Given the failure of the cited prior art to suggest a particulate rSEB vaccine composition comprising dried solid particles having the uniform size distribution recited in the claims, or to even recognize the desirability of such a composition, the present claims are not obvious. Applicants respectfully remind the Examiner that the secondary consideration of unexpected or superior results obtained with an invention provides objective indicia of nonobviousness. See, for example, *In re Mayne*,

104F.3d 1339, 1342, 41USPQ2d 1451, 1454 (Fed. Cir. 1997) and *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990). Such "secondary considerations" further support the conclusion that the rejected claims are not obvious.

In view of the above remarks and the secondary consideration of nonobviousness, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

The Examiner is respectfully requested to withdraw the rejection of the claims. In any event, the Examiner is respectfully requested to consider the above remarks for the purposes of further prosecution. ***Pursuant to 37 C.F.R. § 1.116 and MPEP § 714.12, any claim amendments or arguments that will place the application in condition for allowance may be considered and entered after final rejection.*** The claim amendments and above arguments that were not presented previously were not made earlier because Applicants earnestly believe that the claims were patentable as originally drafted.

Accordingly, in view of the above remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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